

## REMARKS

### Status of the claims

Claims 1-5, 22-28 and 30-61 were previously pending inasmuch as the amendments made in the Response After Final were not entered. Claims 1, 3, 5, 23, 24, 33-35, 38 and 42-52 were withdrawn from consideration.

By amendment herein, claims 22, 49-51 and 58-61 are cancelled without prejudice or disclaimer. In addition, claims 30 and 56 have been amended to make explicit that the recognition region of the zinc finger-binding protein is non-naturally occurring, as described throughout the as-filed specification, for instance in the Examples, particularly Examples 1, 2 and 4. Furthermore, as noted by the Examiner, page 10, lines 17-29 indicates that engineered zinc finger proteins are those not occurring in nature. (See, page 4 of Advisory Action). Withdrawn claim 42 has been amended to indicate that gene expression is modulated in a plant cell.

Accordingly, claims 1-5, 23-28, 30-48 and 52-57 are pending as shown above and claims 2, 4, 25-28, 30-32, 36, 37, 39-41 and 53-54 are under consideration.

### Rejections Withdrawn

Applicants note with appreciation that the rejection of claims 2, 4, 26-28, 30-32, 54 and 55-61 under 35 U.S.C. § 102 over the UMSBP finger of Abeliovich has been withdrawn because this reference does not teach a finger with an alpha helix as required by the claims.

### 35 U.S.C. § 112, first paragraph, written description

Claims 2, 4, 22, 25-28, 30-32, 36, 37, 39-41 and 53-56 were again rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Advisory Action, pages 2-4. The Examiner continues to assert that the “claims do not sufficiently distinguish between naturally occurring and non-naturally occurring proteins and thus a more complete description of naturally (or non-naturally) occurring polypeptides is required.” Advisory Action, page 4.

Applicants again traverse the rejection and supporting remarks.

The pending claims are drawn to non-naturally occurring zinc finger proteins of the specified structure. The claims further indicate that the recognition region of the zinc finger protein also non-naturally occurring and engineered to bind to a target site.

The claimed molecules are clearly described in the as-filed specification. It is axiomatic that satisfaction of the written description requirement does not require that an applicant reiterate what was already known. See, *Falkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006); *Capon v. Eshhar* 76 USPQ2d. 1078 (Fed. Cir. 2005). In the pending case, engineering of the recognition region of a zinc finger protein to bind to a particular target site was known at the time of filing and described in detail on page 10, lines 17-29, including in various references cited therein. Indeed, at the effective filing date of the instant application (January 22, 2001), skilled artisans were aware that the term “engineered zinc finger protein” referred to non-naturally-occurring zinc finger proteins having a binding specificity different from that of any naturally-occurring zinc finger protein, said binding specificity having been determined by the investigator, using empirical selection methods or rational design methods. See, for example, U.S. Patent No. 5,789,538 (Issued August 4, 1998; Reference A26 of IDS mailed on May 9, 2005) at column 8, lines 21-28:

Based on the present disclosure, the skilled artisan will be able to select a wide variety [of] four base pair sequences and engineer zinc fingers which bind specifically to desired four base pair sequence[s]. . . . As a result, a multifingered protein can be engineered such that each finger binds to an adjacent and overlapping subsite.

See, also, U.S. Patent No. 6,013,453 (Issued January 11, 2000; Reference A3 of IDS mailed on April 11, 2003) at column 2, lines 48-54:

Protein engineering experiments have shown that it is possible to alter rationally the DNA-binding characteristics of individual zinc fingers when one or more of the  $\alpha$ -helical positions is varied in a number of proteins [references omitted].

See, also, WO 00/41566 (published July 20, 2000; Reference B20 of IDS mailed on May 9, 2005) at page 22, lines 14-15:

The ZFPs [zinc finger proteins] of the invention are engineered to recognize a selected target site in the endogenous gene of choice.

These and other references, which were available on the priority date of the subject application, show that one of skill in the art would have understood that Applicants were in possession of non-naturally-occurring proteins whose amino acid sequence in the recognition region had been engineered to bind to a target nucleotide sequence of choice, as claimed.

Furthermore, with respect to the term “non-naturally occurring” Applicants also note that the Board of Patent Appeals and Interferences has recently reaffirmed that the term “naturally occurring” would be understood by the persons of skill in the art to mean that it exists or is found in nature. *See*, page 3 of Appendix A: *Ex parte Dewis et al.* (2007) Appeal 2007-1610 (BPAI). Thus, in the instant case, the skilled artisan would readily understand that the term “non-naturally occurring” refers to a zinc finger containing a recognition region that does not occur in nature.

Thus, when properly construed, the claims are adequately described, as set forth above and acknowledged by the Office. Accordingly, the rejection should be withdrawn.

### 35 U.S.C. § 102

The rejection of claims 2, 4, 26-28, 30-32 and 54 as allegedly anticipated by Green was maintained. Advisory Action, pages 4-5. Green was alleged to disclose construction of mutants of zif268 in which each of the three constituent zinc fingers was converted from its naturally-occurring C<sub>2</sub>H<sub>2</sub> (CCHH) configuration to a C<sub>4</sub> (CCCC) configuration. *Id.*

As noted above, the claims require that the claimed polynucleotides encode a zinc finger protein in which the recognition region is non-naturally occurring and has been engineered to bind to a target sequence. By contrast, Green clearly indicates that the recognition region of the proteins is unaltered and remains as the naturally occurring Zif268 sequences. Green simply used a known protein (zif268) that binds a known target

sequence, altered certain zinc-coordinating residues, and tested the mutant proteins for their ability to bind to the same target sequence.

Since Green does not describe or demonstrate non-naturally occurring zinc finger proteins comprising non-naturally occurring, engineered recognition domains as claimed, the rejection is improper and should be withdrawn.

### **35 U.S.C. § 103**

The Advisory Action indicated that the arguments directed to rejections under 103 were not addressed because the amendments after final were not entered. Advisory Action, page 5.

The rejections under 35 U.S.C. § 103 are all based on Green, which as noted above, fails entirely to teach or suggest zinc finger proteins in which the recognition region is non-naturally occurring and has been engineered to bind to a target site. Indeed, the entire point of Green was to test the ability of a naturally occurring recognition region to bind to its cognate target site when certain zinc coordinating residues in the backbone region were modified. Therefore, Green teaches away from proteins containing engineered recognition regions as claimed and there is no combination of Green with any of the other cited references that would result in the claimed subject matter. Accordingly, the rejections should be withdrawn.

**CONCLUSION**

In light of the amendments and remarks presented herein, it is believed that the elected subject matter is in condition for allowance. Applicants therefore request examination of generic subject matter. If the Examiner believes that a telephone conversation would expedite prosecution, she is invited to contact the undersigned at the telephone number given below.

Respectfully submitted,

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